

PATENT Attorney Docket No. UM-08550

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Joseph Holoshitz *et al.*

Serial No.: 10/786,774

Group No.: 1649 Examiner: Standley, S. Filed: 02/25/04

Entitled: Methods And Compositions For The Treatment Of

Diseases Associated With Signal Transduction

Abberrations

INFORMATION DISCLOSURE STATEMENT TRANSMITTAL

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.10

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service in an envelope as "Express Mail Post Office to Addressee" Mailing Label Number EV769933010US, addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Dated: January 12, 2006

Sir:

Enclosed please find an Information Disclosure Statement and Form PTO-1449, including copies of the references contained thereon, for filing in the U.S. Patent and Trademark Office.

A check for \$180.00 is also enclosed pursuant to 37 C.F.R. § 1.17(p) for filing this Information Disclosure Statement after three months as set forth in 37 C.F.R. § 1.97(c).

The Commissioner is hereby authorized to charge any additional fee or credit overpayment to our Deposit Account No. 08-1290. An originally executed duplicate of this transmittal is enclosed for this purpose.

Dated: January 12, 2006

Thomas W. Brown Registration No. 50,002

MEDLEN & CARROLL, LLP 101 Howard Street, Suite 350 San Francisco, California 94105 617/984.0616





IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Joseph Holoshitz et al.

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Dated: January 12, 2006

Sir:

The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

In compliance with 37 C.F.R. § 1.98(a)(2) the applicant has not provided hard copies of cited U.S. Patents since the instant application was filed after June 30, 2003.

The following printed publications are referred to in the body of the specification:

- U.S. Patent No. 4,552,891 to Ho et al.;
- U.S. Patent No. 4,588,394 to Schulte et al.;
- U.S. Patent No. 4,902,505 to Pardridge et al.;
- U.S. Patent No. 5,004,697 to Pardridge;
- U.S. Patent No. 5,051,448 to Shashoua;
- U.S. Patent No. 5,130,129 to Pardridge;
- U.S. Patent No. 5,147,855 to Gozes et al.;
- U.S. Patent No. 5,166,320 to Wu et al.;
- U.S. Patent No. 5,169,862 to Burke, Jr. et al.;
- U.S. Patent No. 5,192,746 to Lobl et al.;
- U.S. Patent No. 5,354,844 to Beug et al.:

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- U.S. Patent No. 5,393,773 to Craig *et al.*;
- U.S. Patent No. 5,525,727 to Bodor;
- U.S. Patent No. 5,539,085 to Bischoff et al.;
- U.S. Patent No. 5,554,639 to Craig *et al.*;
- U.S. Patent No. 5,559,103 to Gaeta et al.;
- U.S. Patent No. 5,576,423 to Aversa *et al.*;
- U.S. Patent No. 5,601,835 to Sabel *et al.*;
- U.S. Patent No. 5,618,803 to Bodor;
- U.S. Patent No. 5,643,207 to Rise;
- U.S. Patent No. 5,624,894 to Bodor;
- U.S. Patent No. 5,670,477 to Poduslo *et al.*;
- U.S. Patent No. 5,801,161 to Merkus;
- U.S. Patent No. 5,864,037 to Chasin *et al.*;
- U.S. Patent No. 5,869,479 to Kreutner *et al.*;
- U.S. Patent No. 5,972,883 to Gozes et al.;
- U.S. Patent No. 6,042,579 to Elsberry *et al.*;
- U.S. Patent No. 6,117,454 to Kreuter *et al.*;
- U.S. Patent No. 6,132,764 to Li *et al.*;
- U.S. Patent No. 6,153,193 to Kabanov *et al.*;
- U.S. Patent No. 6,172,277 to Tate *et al.*;
- U.S. Patent No. 6,179,826 to Aebischer *et al.*;
- Auger et al.,"HLA-DR4 and HLA-DR10 Motifs That Carry Susceptibility To Rheumatoid Arthritis Bind 70-kD Heat Shock Proteins," Nature Med 2:306-310 (1996);
- Basu S. et al., "CD91 is a common receptor for heat shock proteins gp96, hsp70, and calreticulin," *Immunity* 14: 303-313 (2001);
- Benvenisty and Reshef,"Direct introduction of genes into rats and expression of the genes" *Proc. Nat. Acad. Sci. USA*, 83:9551-55 (1986);
- Bickel et al., "Pharmacologic effects in vivo in brain b yvector-mediated peptide drug delivery," Proc. Natl. Acad. Sci. USA 90:2618-2622 (1993);
- Borisova et al., "Behavior of a Short preS1 Epitope on the Surface of Hepatitis B
 Core Particles," Biol Chem 380:315-324 (1999);
- Colaco CB et al.,"Deficient repair of O⁶ -methylguanine in lympocytes from rheumatoid arthritis families may be and acquired defect," Clin Exp Immunol 72:15-19 (1988);

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- Corder EH *et al.*,"Gene Dose of Apolipoprotein E Type 4 Allele and the Risk of Alzheimer's Disease in Late Onset Families," *Science* 261:921-923 (1993);
- Curran M et al.,"HLA-DR antigens associated with major genetic risk for lateonset Alzheimer's disease," NeuroReport 8:1467-1469 (1997);
- Dubensky et al., "Direct transfection of viral and plasmid DNA into the liver or spleen of mice," Proc. Nat. Acad. Sci. USA, 81:7529-33 (1984);
- Eldred *et al.*, "Orally Active Non-Peptide Fibrinogen Receptor (GpIIb/IIIa) Antagonists: Identification of 4-[4-[4-(Aminoiminomethyl)phenyl]-1-piperazinyl]-1-piperidineacetic Acid as a Long-Acting, Broad-Spectrum Antithrombotic Agent," *J. Med. Chem.* 37:3882 (1994);
- Fisher *et al.*,"(±)-cis-2-Methyl-spiro (1,3-oxathiolane-5,3') quinuclidine (AF102B): a new M₁ agonist attenuates cognitive dysfunctions in AF64A-treated rats," *Neurosci Lett* 102:325-331 (1989);
- Forsythe and Westbrook,"Slow Excitatory Postsynaptic Currents Mediated By N-Methyl-D-Aspartate Receptors On Cultured Mouse Central Neurones," J Physiol (Lond) 396:515-533 (1988);
- Galea E and Feinstein DL., "Regulation of the expression of the inflammatory nitric oxide synthase (NOS2) by cyclic AMP," FASEB J 13:2125-2137 (1999);
- Greegersen PK et al.,"The Share Epitope Hypothesis: An Approach to Understanding The Molecular Genetics of Susceptibility to Rheumatoid Arthritis," Arthritis Rheum 30:1205-1213 (1987);
- Ku et al.,"Potent Non-peptide Fibrinogen Receptor Antagonists Which Present An Alternative Pharmacohore," J. Med. Chem. 38:9 (1995);
- Levitzki A.,"Targeting signal transduction for disease therapy," Curr Opin Cell Biol 8:239-244 (1996);
- Linden *et al.*,"Characterization of Human A_{2B} Adenosine Receptors: Radiogland Binding, Western Blotting, and Coupling to G_q in Human Embryonic Kidney 293 Cells and HMC-1 Mast Cells," *Molecular Pharmacology* 56:705-713 (1999);
- Lipman and Pearson,"Rapid and Sensitive Protein Similarity Searches," *Science* 227:1435-1441 (1985);
- McCurdy D et al.,"Delayed Repair of DNA Damage by Ionizing Radiation in Cells from Patients with Juvenile Systemic Lupus Erythematosus and Rheumatoid Arthritis," Radiat Res 147:48-54 (1997);

- Nepom GT et al.,"HLA Genes Associated With Rheumatoid Arthritis:
 Identification of Susceptibility Alleles Using Specific Oligonucleotide Probes,"
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- Pearson and Lipman,"Improved tools for biological Sequence comparison," *Proc. Natl. Acad. Sci. (USA)* 85:2444-2448 (1988);
- Pericak-Vance MA et al., "Linkage Studies in Familial Alzheimer Disease:
 Evidence for Chromosome 19 Linkage," Am J Hum Genet 48:1034-1050 (1991);
- Pumpens P and Grens E.,"Hepatitis B core particles as a universal display model: a structure-function basis for development," *FEBS Lett* 442:1-6 (1999);
- Stirttmatter WJ and Roses AD,"Apolipoprotein E and Alzheimer disease," *Proc Natl Acad Sci USA* 92:4725-4727 (1995);
- Wagner, et al., "Transferin-polycation-DNA complexes: The effect of polycations on the structure of the complex and DNA delivery to cells," Proc. Natl. Acad. Sci., 88:4255-4259 (1991);
- Weisgraber KH., "Apolipoprotein E distribution among human plasma lioproteins: role of the cysteine-arginine interchange at residue 112," *J Lipid Res* 31:1503-1511 (1990);
- Weyand CM et al., "The Influence of HLA-DRB1 Genes on Disease Severity in Rheumatoid Arthritis," Ann Intern Med 117:10 801-806 (1992); and
- Wolff *et al.*,"Direct Gene Transfer Into Mouse Muscle in Vivo," *Science*, 247:1456-68 (1990).

The following documents have been cited by the examiner in the parent application, Application No. 10/161,959, filed on 6/30/02:

- U.S. Patent No. 6,153,200 to Carson *et al.*;
- WIPO No. 97/34002 to Carson *et al*.
- WIPO No. 90/14835 to Carson *et al*.
- Walker et al.,"Proteopathy: The next therapeutic frontier?," Curr Opin Investig Drugs, 3(5):782-787 (2002);
- Fitjohn et al.,"Age-related impairment of synaptic transmission but normal long-term potentiation in transgenic mice that overexpress the human APP695SWE mutant form of amyloid precursor protein," J. Neuroscience, 21(13):4691-4698 (2001);
- Chapman *et al.*,"Impaired synaptic plasticity and learning in aged amyloid precursor protein transgenic mice," *Nature Neuroscience*, 2:271-276 (1999);

- Schenk et al., "Potential treatment opportunities for alzheimer's disease through inhibition of secretases and Aβ immunization," J. Mole. Neuroscience, 17:259-267 (2001);
- Perdriger et al.,"Role of HLA-DR-DR and DR-DQ associations in the expression of extraarticular manifestations and rheumatoid factor in rheumatoid arthritis," J. Rheumatology, 24(7):1272-1276 (1997);
- Auger et al.,"A function for the QKRAA amino acid motif: mediating binding of DnaJ to DnaK," J. Clin Invest, 99(8):1818-1822 (1997);
- Singal *et al.*,"Genetics of rheumatoid arthritis (RA): two separate regions in the major histocompatibility complex contribute to susceptibility to RA," *Immunology Letters*, 69:301-306 (1999).

The following documents were provided to the examiner with an office action response from the parent application, Application No. 10/161,959, filed on 6/30/02:

- Vitolo *et al.*,"Amyloid β-peptide inhibition of the PKA/CREB pathway and long-term potentation: reversibility by drugs that enhance cAMP signaling," *PNAS*, 99(20):13217-13221 (2002);
- Sun *et al.*,"Bilateral injection of isoproterenol into hippocampus induces alzheimer-like hyperphosphorylation of tau and spatial memory deficit in rat," *FEBS Letters*, 579:251-258 (2005);
- Gong *et al.*,"Persistent improvement in synaptic and cognitive functions in an alzheimer mouse model after rolipram treatment," *J. Clin. Invest.*, 114(11):1624-1634 (2004).

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: January 12, 2006

Thomas W. Brown Registration No. 50.002

MEDLEN & CARROLL, LLP 101 Howard Street, Suite 305 San Francisco, California 94105 617.984.0616



ORM PTO-14 Modified)	137	S. J. S.	U.S. Depar Patent and	tment of Commerce Trademark Office	Attorney Docket No	.: UM-08550	Serial No.: 10	/786,774
			FATEMENT BY APPLICANT is If Necessary)		Applicant: Joseph Holoshitz et al.			
				Filing Date: 02/25/04		04	Group Art Unit: 1649	
				U.S. PATENT DOC	UMENTS			
Examiner Initials	Cite No.	Serial / Patent Number	Issue Date	Applicant / Patentee		Class	Subclass	Filing Date
	1	4,552,891	11/12/85	I	lo et al.	514	443	9/13/83
,	2	4,588,394	05/13/86	Sch	nulte <i>et al</i> .	604	9	03/16/84
-	3	4,902,505	2/20/90	Pard	ridge et al.	424	85.7	4/25/88
	4	5,004,697	4/02/91	Pa	ardridge	436	547	8/17/87
	5	5,051,448	9/24/91	s	hashoua	514	547	5/07/90
	6	5,130,129	7/14/92	Pa	ardridge	424	85.8	3/06/90
	7	5,147,855	9/15/92	Go	ozes et al.	514	12	7/07/89
	8	5,166,320	11/24/92	v	Vu <i>et al</i> .	530	395	04/02/90
	9	5,169,862	12/08/92	Ві	irke <i>et al</i> .	514	450	11/18/91
	10	5,192,746	3/09/93	L	obl et al.	514	11	7/09/90
	11	5,354,844	10/11/94	В	eug et al.	530	345	03/09/90
	12	5,393,773	2/28/95	Cı	aig et al.	514	415	1/19/92
	13	5,525,727	6/11/96		Bodor	546	39	10/28/92
	14	5,539,085	7/23/96	Bise	choff et al.	530	350	8/20/93
	15	5,554,639	9/10/96	Cr	aig <i>et al</i> .	514	415	6/02/95
	16	5,559,103	9/24/96	Ga	eta <i>et al</i> .	514	54	7/20/94
	17	5,576,423	11/19/96	Av	ersa et al.	530	388.75	12/02/94
	18	5,601,835	2/11/97	Sa	bel <i>et al</i> .	424	424	1/12/94
	19	5,618,803	4/08/97		Bodor	514	81	11/15/94
	20	5,643,207	07/01/97		Rise	604	93	06/27/96
	21	5,624,894	4/29/97		Bodor	514	2	4/27/95
	22	5,670,477	9/23/97	Pod	uslo <i>et al</i> .	514	2	4/20/95
	23	5,801,161	9/01/98	I	Merkus	514	52	6/17/96
	24	5,864,037	1/26/99	Ch	asin <i>et al</i> .	544	118	6/06/96
	25	5,869,479	2/09/99	Kre	utner et al.	514	212	8/14/97
	26	5,972,883	10/26/99	Gozes et al. Elsberry et al.		514	12	3/30/95
	27	6,042,579	03/28/00			604	891.1	04/30/97
	28	6,117,454	9/12/00	Kre	ıtner et al.	424	490	5/27/97
	29	6,132,764	10/17/00	1	i et al.	424	450	4/08/96
	30	6,153,193	11/28/00	Kabanov et al.		424	184.1	6/07/95
	31	6,172,277	01/09/01	Tate et al.		800	12	10/28/97
	32	6,179,826	1/30/01	Aebi	scher et al.	604	522	10/29/96
	33	6,153,200	11/2000	Car	son et al.	424	201.1	
aminer:					Date Considered:			

EXAMINER:

Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 U.S. Department of Commerce Serial No.: 10/786,774 Attorney Docket No.: UM-08550 Patent and Trademark Office (Modified) INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use Several Sheets If Necessary) Applicant: Joseph Holoshitz et al. Group Art Unit: 1649 Filing Date: 02/25/04 (37 CFR § 1.98(b)) FOREIGN PATENTS OR PUBLISHED FOREIGN PATENT APPLICATIONS Translation Document Subclass **Publication Date** Country / Patent Office Class Number Yes No 18.09.97 WO 97/34002 WIPO A61K 37/02 34 15/31 WIPO C12N 35 WO 90/14835 13.12.90 OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication) Auger 1 et al., "HLA-DR4 and HLA-DR10 Motifs That Carry Susceptibility To Rheumatoid Arthritis Bind 70-kD Heat Shock Proteins," Nature Med 2:306-310 (1996) 36 37 Basu S. et al., "CD91 is a common receptor for heat shock proteins gp96, hsp70, and calreticulin," Immunity 14: 303-313 (2001) 38 Benvenisty and Reshef, "Direct introduction of genes into rats and expression of the genes" Proc. Nat. Acad. Sci. USA, 83:9551-55 (1986) Bickel et al.,"Pharmacologic effects in vivo in brain b yvector-mediated peptide drug delivery," Proc. Natl. Acad. Sci. USA 90:2618-2622 39 40 Borisova et al., "Behavior of a Short preS1 Epitope on the Surface of Hepatitis B Core Particles," Biol Chem 380:315-324 (1999) Colaco CB et al.,"Deficient repair of O⁶ -methylguanine in lympocytes from rheumatoid arthritis families may be and acquired defect," Clin Exp Immunol 72:15-19 (1988) 41 Corder EH et al., "Gene Dose of Apolipoprotein E Type 4 Allele and the Risk of Alzheimer's Disease in Late Onset Families," Science 261:921-923 (1993) 42 43 Corder EH et al., "Protective effect of apolipoprotein E type 2 allele for late onset Alzheimer disease," Nat Genet 7:180-184 (1994) 44 Curran M et al.,"HLA-DR antigens associated with major genetic risk for late-onset Alzheimer's disease," NeuroReport 8:1467-1469 (1997) Dubensky et al.,"Direct transfection of viral and plasmid DNA into the liver or spleen of mice," Proc. Nat. Acad. Sci. USA, 81:7529-33 (1984) 45 Eldred et al., "Orally Active Non-Peptide Fibrinogen Receptor (Gpllb/Illa) Antagonists: Identification of 4-[4-[4-(Aminoiminomethyl)phenyl]-1-piperazinyl]-1-piperidineacetic Acid as a Long-Acting, Broad-Spectrum Antithrombotic Agent," J. Med. Chem. 37:3882 (1994) 46 Fisher et al.,"(±)-cis-2-Methyl-spiro (1,3-oxathiolane-5,3') quinuclidine (AF102B): a new M₁ agonist attenuates cognitive dysfunctions in AF64A-treated rats," Neurosci Lett 102:325-331 (1989) 47 Forsythe and Westbrook, "Slow Excitatory Postsynaptic Currents Mediated By N-Methyl-D-Aspartate Receptors On Cultured Mouse Central Neurones," J Physiol (Lond) 396:515-533 (1988) 48 Galea E and Feinstein DL., "Regulation of the expression of the inflammatory nitric oxide synthase (NOS2) by cyclic AMP," FASEB J 13:2125-2137 (1999) 49 Greegersen PK et al.,"The Share Epitope Hypothesis: An Approach to Understanding The Molecular Genetics of Susceptibility to Rheumatoid Arthritis," Arthritis Rheum 30:1205-1213 (1987) 50 51 Ku et al., "Potent Non-peptide Fibrinogen Receptor Antagonists Which Present An Alternative Pharmacohore," J. Med. Chem. 38:9 (1995) 52 Levitzki A., "Targeting signal transduction for disease therapy," Curr Opin Cell Biol 8:239-244 (1996) Linden et al., "Characterization of Human A_{3B} Adenosine Receptors: Radiogland Binding, Western Blotting, and Coupling to G_q in Human Embryonic Kidney 293 Cells and HMC-1 Mast Cells," Molecular Pharmacology 56:705-713 (1999) 53 54 Lipman and Pearson, "Rapid and Sensitive Protein Similarity Searches," Science 227:1435-1441 (1985) McCurdy D et al.,"Delayed Repair of DNA Damage by Ionizing Radiation in Cells from Patients with Juvenile Systemic Lupus Erythematosus and Rheumatoid Arthritis," Radiat Res 147:48-54 (1997) 55 Nepom GT et al.,"HLA Genes Associated With Rheumatoid Arthritis: Identification of Susceptibility Alleles Using Specific Oligonucleotide Probes," Arthritis Rheum 32:15-21 (1989) 56 57 Pearson and Lipman, "Improved tools for biological Sequence comparison," Proc. Natl. Acad. Sci. (USA) 85:2444-2448 (1988) Pericak-Vance MA et al.,"Linkage Studies in Familial Alzheimer Disease: Evidence for Chromosome 19 Linkage," Am J Hum Genet 48:1034-1050 (1991) 58 Pumpens P and Grens E., "Hepatitis B core particles as a universal display model: a structure-function basis for development," FEBS Lett 442:1-6 (1999) 59 Date Considered: Examiner: **EXAMINER:** Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 (Modified)		U.S. Department of Commerce Patent and Trademark Office	Attorney Docket No.: UM-08550	Serial No.: 10/786,774					
INFORMATION DISCLOSURE STATEMENT BY APPLICAN (Use Several Sheets If Necessary)			Applicant: Joseph Holoshitz et al.						
(37 CFR § 1.98		(Ose several slices if Necessary)	Filing Date: 02/25/04	Group Art Unit: 1649					
	OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)								
	60	Stirttmatter WJ and Roses AD, "Apolipoprotein E and Alzheimer disease," Proc Natl Acad Sci USA 92:4725-4727 (1995)							
	61	Wagner, et al.,"Transferin-polycation-DNA complexes: The effect of polycations on the structure of the complex and DNA delivery to cells," Proc. Natl. Acad. Sci., 88:4255-4259 (1991)							
	62	Weisgraber KH., "Apolipoprotein E distribution among human p Lipid Res 31:1503-1511 (1990)	aber KH., "Apolipoprotein E distribution among human plasma lioproteins: role of the cysteine-arginine interchange at residue 112," J es 31:1503-1511 (1990)						
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_	67	Chapman et al.,"Impaired synaptic plasticity and learning in aged amyloid precursor protein transgenic mice," Nature Neuroscience, 2:271-276 (1999)							
	68	Schenk et al., "Potential treatment opportunities for alzheimer's disease through inhibition of secretases and Aβ immunization," J. Mole. Neuroscience, 17:259-267 (2001)							
	69	Perdriger et al., "Role of HLA-DR-DR and DR-DQ associations in the expression of extraarticular manifestations and rheumatoid factor in rheumatoid arthritis," J. Rheumatology, 24(7):1272-1276 (1997)							
	70	Auger et al.,"A function for the QKRAA amino acid motif: medi	iating binding of DnaJ to DnaK," J. Clin In	vest, 99(8):1818-1822 (1997)					
	7 1	Singal et al.,"Genetics of rheumatoid arthritis (RA): two separate regions in the major histocompatibility complex contribute to susceptibility to RA," Immunology Letters, 69:301-306 (1999)							
	72	Vitolo et al.,"Amyloid β-peptide inhibition of the PKA/CREB pathway and long-term potentation: reversibility by drugs that enhance cAMP signaling," PNAS, 99(20):13217-13221 (2002)							
	73	Sun et al.,"Bilateral injection of isoproterenol into hippocampus induces alzheimer-like hyperphosphorylation of tau and spatial memory deficit in rat," FEBS Letters, 579:251-258 (2005)							
	74	Gong et al.,"Persistent improvement in synaptic and cognitive full 114(11):1624-1634 (2004)	unctions in an alzheimer mouse model after	rolipram treatment," J. Clin. Invest.,					
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